REVIEW ARTICLE

A COMPLETE REVIEW ON ACNE VULGARIS

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ABSTRACT:
Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units. It is a pleomorphic disorder with multifactorial pathogenesis. The many expressions of acne rarely present a diagnostic challenge, but correct classification of acne is crucial in choosing the appropriate therapies. Although previous research has provided a better understanding of the pathogenic factors, there is still a great deal to be learned. Obstruction of follicles causes follicular distention, which is often accompanied by the proliferation of the bacteria Propionibacterium acnes and the activation of an inflammatory response. Although the diagnosis of acne is usually straightforward, some conditions are occasionally confused with acne, including periorificial dermatitis, keratosis pilaris, angiofibromas, bacterial folliculitis, and demodex folliculitis. In addition to physical discomfort, acne is associated with considerable psychological distress, limitation of activities, and increased risk of depression and suicide.
Key Words: Acne Vulgaris, Pathophysiology, Treatment

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INTRODUCTION

Acne vulgaris (or simply acne) is a long-term skin condition characterized by areas of blackheads, whiteheads, pimples, greasy skin, and possibly scarring. The resulting appearance may lead to anxiety, reduced self-esteem, and in extreme cases, depression or thoughts of suicide.[1]

Genetics is estimated to be the cause of 80% of cases. The role of diet as a cause is unclear. Neither cleanliness nor sunlight appear to be involved. However, cigarette smoking does increase the risk of developing acne and worsens its severity. Acne mostly affects skin with a greater number of oil glands including the face, upper part of the chest, and back. During puberty in both sexes, acne is often brought on by an increase in androgens such as testosterone. Excessive growth of the bacteria Propionibacterium acnes, which is normally present on the skin, is often involved.[2, 3]

Many treatment options are available to improve the appearance of acne including lifestyle changes, procedures, and medications. Eating fewer simple carbohydrates like sugar may help. Topical benzoyl peroxide, salicylic acid, and azelaic acid are commonly used treatments.[4] Antibiotics and retinoids are available topically and by mouth to treat acne. However, resistance to antibiotics may develop. A number of birth control pills may be useful in women. Oral isotretinoin is usually reserved for severe acne due to greater potential side effects. Early and aggressive treatment is advocated by some to lessen the overall long-term impact to individuals.[5]

LESION TYPES

There are two major types of acne lesions: noninflammatory and inflammatory. Although most drug products for acne are intended for the broad indication of acne vulgaris, some products have been developed that only target one of these two specific subsets of acne vulgaris lesions.[6]

Noninflammatory lesions of acne are the open (blackheads) or closed (whiteheads) comedones.

Closed comedones may be more difficult to detect visually and may require stretching of the skin to aid in visualization. These lesions, especially closed comedones, may be precursors to the larger inflammatory lesions and therefore are of clinical importance.

Inflammatory lesions are divided into papules, pustules, and nodules/nodulocystic lesions, depending on the severity and location of the inflammation within the dermis. The papules and pustules have surrounding halos of erythema allowing for their characterization as inflammatory. Nodules are typically erythematous and often tender and/or painful. Additionally, they are deep-seated in the skin (i.e., centered in the dermis or subcutis). Nodules have been defined as being greater than 5 mm in diameter. The borders of these lesions may be difficult to determine because of the associated erythema/inflammation.

CLINICAL MANIFESTATION

The lesions of acne occur predominantly on the face and to a lesser extent on the back and the chest.[7] The condition usually begins at puberty, when slight degrees of acne are common and are regarded as being physiological. Both sexes are affected with equal frequency. The condition diminishes in severity from the age of 20 years and tends to disappear around the age of 25, although occasionally it can persist throughout life. Its course is variable and recurrent exacerbations are common. In younger patients it more commonly affects the face, while in the middle-aged the back is the principal site. Certain diseases which occlude the follicular pores, for example hidradenitis suppurativa and necrotising cellulitis of the scalp, may be associated with acne. Severe acne variants are comparatively rare but they are clinically important. Four main variants are recognised:[8] Pyoderma faciale is seen usually in an older woman with existing acne who is subjected to stress, when a localised but explosive pattern of the disease appears. Acne conglobata is a severe form of the disease which affects the face, back and limbs. Cystic and pustular lesions occur and scarring may be marked. It occurs mainly in men. Acne fulminans is an immunologically induced severe systemic variant of acne conglobata. The clinical features are those of acne conglobata plus the classic delayed hypersensitivity systemic reaction with splenomegaly, arthropathy and rashes. Gram-negative folliculitis is associated with the long-term antibiotic treatment of acne. Acne which was well controlled suddenly appears to "escape" from control. This condition takes the form of a sudden eruption of small follicular pustules.

PATHOGENESIS

Acne is a complex disease with multifactorial pathogenesis and considerable variation in severity. Thus,therapy can be directed at multiple factors and modifiedfor individual patients.

Acne is a disorder of the sebaceous follicles, which are special pilosebaceous units located on the face, neck, chest, upper back, and upper arms. These units consist of relatively large sebaceous glands associated with small hair follicles. Acne arises from the interaction of 4 factors:[9]

Comedogenesis—sebaceous follicle obstruction arising from increased cohesiveness of follicular epithelial cells, hyperproliferation of ductal keratinocytes, or both.

Excessive sebum production caused by androgenic stimulation of sebaceous glands at or around adrenarche or later.

Proliferation of Propionibacterium acnes, an anaerobic diphtheroid that populates sebaceous follicles and is a normal constituent of cutaneous flora. P acnes produce chemotactic factors and proinflammatory mediators that may lead to inflammation.

Inflammation is a direct or indirect result of Pacnes proliferation. Follicular rupture and extension of inflammation into the dermisresult in formation of the inflammatorylesions of acne vulgaris—papules, pustules, and nodules.

THE BRAIN-GUT-SKIN THEORY[10]

Drawing on several lines of experimental evidence and clinical anecdotes, Stokes and Pillsbury provided a ‘theoretical and practical consideration of a gastrointestinal mechanism’ for ways in which the skin is influenced by emotional and nervous states. These authors connected emotional states - depression, worry and anxiety – to altered gastrointestinal tract function, changes that cause alterations to the microbial flora, which they theorized, in turn promotes local and systemic inflammation.Stokes and Pillsbury suggested that stress-induced alterations to microbial flora could increase the likelihood of intestinal permeability,

which in turn sets the stage for systemic and local skin inflammation. The remedies these authors discussed as a means to cut off the stress-induced cycle included the 'direct introduction of acidophil organisms in cultures such as those of Bacillus acidophilus'.

CONTEMPORARY EVIDENCE[11]

In recent years it has been confirmed that hypochlorhydriais a significant risk factor for small intestinal bacterial over growth (SIBO). Indeed SIBO is detected via hydrogen breath testing in half of patients on long-term proton pump inhibitor treatment. SIBO presents itself on a wide continuum between being asymptomatic and, at its extreme, a severe malabsorption syndrome.

For many, there may be very mild gastrointestinal symptoms, including bloating, diarrhea, abdominal pain, and constipation. It is also reported to be prevalent infunctional syndromes such as fibromyalgia and chronic fatigue syndrome. One older study using a bismuth test beverage and objective fluoroscopy did report intestinal stagnation in 47% of a small group of acne

(n = 30) acne patients. They also reported constipationas a clinical complaint in 40% of acne patients.

Even if constipation were more frequent, as the recent population study involving 13,000 adolescents indicates, it would be tempting to dismiss it as having no relevance whatsoever to the pathogenesis of acne and/or depression. Yet, an important study in 2005 should provide cause for further consideration; among 57 patients with functional constipation, fecal concentrations of Lactobacillus and Bifidobacterium were significantly lower and intestinal permeability was significantly higher compared to healthy adults without constipation.

INTESTINAL MICROFLORA[12]

The Stokes-Pillsbury theory was also predicated upon changes not only to the residential location of microbes within the intestinal tract, they suspected that a quantitative alteration to the microrobial flora was also at play. Most notable are stress-induced reductions in Lactobacillus and Bifidobacteria species.

The potential of stress-induced changes to the gastrointestinal microflora among acne patients has sadly received little attention. With recent advances in molecular identification of intestinal microbial inhabitants, we are hopeful that investigators will take a renewed interest in potential changes to the enteric microbial profile among acne patients.

PROBIOTIC ADMINISTRATION[13]

As mentioned, Stokes and Pillsbury made numerous references to the use of L. acidophilus and L. acidophilus- fermented milk products as a treatment modality in the context of the brain-gut-skin inflammatory process.Indeed, other physicians writing in the 1930s madereference to the popularity of L. acidophilus cultures among the general public as an internal means to treat acne. However, despite the apparent appeal of what would later be described as probiotics, there was little research to determine efficacy.

The theoretical value of oral probiotics as adjuvant care in acne vulgaris seems sound. Recent studies have shown that orally consumed pre and probiotics can reduce systemic markers of inflammation and oxidative stress. Since the local burden of lipid peroxidation in acne is high, such that it appears to place a great demand upon blood-derived antioxidants, the ability of oral probiotics to limit systemic oxidative stress may be an important therapeutic pathway. Oral probiotics can regulate the release of inflammatory cytokines within the skin, and a specific reduction in interleukin-1 alpha (IL-1-a), noted under certain experimental conditions, would certainly be of potential benefit in acne.

THE RELATIONSHIP BETWEEN ACNE AND DIET[14]

There are several common misconceptions about the causes or treatment of acne. Many people think that acne is caused by dirt, and that intensive scrubbing of the skin can cure acne. However, vigorous scrubbing or abrasive cleansers do not improve acne, and may actually worsen it by traumatizing the skin and exacerbating inflammation.[15] The relationship between acne and diet is controversial. Acne is often attributed to several dietary causes, including chocolate, soda, sweets, or fried foods, although many acne experts have argued that diet is not a significant contributor to acne.In particular, researchers have noted that acne is nearly absent in regions where the diet consists primarily of minimally processed plant or animal foods and very low amounts of western-style high-carbohydrate foods that yield very high glycemic loads when ingested. Diet-related hyperinsulinemia may also

contribute to acne by stimulating androgen production. The relationship between acne and the consumption of dairy products and other foods was examined using data from the Nurses' Health Study II, a long-term, ongoing prospective study that is examining associations among several lifestyle factors and illnesses among women who were between the ages of 25 and 42 years. Results showed that Acne was also significantly associated with more frequent consumption of several other dairy products, including instant breakfast drink, sherbet, cream cheese, and cottage cheese.[16]

The authors noted that milk contains numerous proteins that might potentially influence acne risk, including estrogens, progesterone, androgens and androgen precursors, IGF-1, and others. They also hypothesized that differences in processing between whole milk and skim milk might affect acne risk by altering the bioavailability of some of the hormonal components of milk. For example, they noted that whole milk contains more estrogen than skim milk, and that estrogens may exert a protective effect against acne. Although these results provide some evidence for an association between acne and the consumption of dairy products during adolescence, a significant limitation of this study was that it relied entirely on participants' retrospective recall of diet and acne diagnosis.

TREATMENT ASPECTS[17]

Mild-to-Moderate Acne: Topical Antibiotics

Topical antibiotics including erythromycin and clindamycin, are effective and well tolerated for the treatment of acne vulgaris. However, because antibiotics may potentially decrease sensitivity of P. acnes, the use of these agents should be limited. Topical antimicrobial combination therapy is more effective than monotherapy.

Mild-to-moderate Acne: Topical Retinoids

The available topical retinoids used for acne vulgaris include tretinoin (Retin-A®), adapalene (Differin®) and tazarotene (Tazorac®). These agents work by reducing obstruction within the follicle. Such products are considered first-line for the treatment of mild-to-moderate inflammatory acne and comedonal acne. Additionally, these agents are preferred for maintenance therapy of acne in order to preserve the use of antibiotics.

Mild-to-moderate Acne: Combination therapy

Recent guidelines suggest that combination therapy with topical retinoids and antimicrobial agents achieves significantly greater and faster clearing of acne compared with antimicrobial therapy alone.Combination therapies utilize agents with complimentary mechanisms of action to target multiple etiological factors simultaneously.

Mild-to-Moderate Acne: Hormonal Therapy

Hormonal therapy produces anti-androgen effects, which leads to a decrease in testosterone circulating in the body. Consequently, sebaceous gland stimulation is prevented, reducing sebum production. FDA-approved hormonal therapies consist of oral contraceptive agents that contain norgestimate with ethinyl estradiol (Ortho-Tri-Cyclen®) and norethindrone acetate with ethinyl estrodial (Estrostep®), as well as the anti-androgenic agent, spironolactone.

Severe Acne: Oral Isotretinoin

Isotretinoin (Accutane®) is a naturally occurring metabolite of Vitamin A, and is indicated for the treat-ment of severe acne. Isotretinoin works by reducing the size of the sebaceous gland, suppressing sebum production, and normalizing follicular epithelial desquamation. Several studies show isotretinoin to be effective in severe acne. In a randomized controlled trial with 76 patients, isotretinoin showed an 80% reduction in total acne after 4 months. Treatment doses ranged from 0.1mg/kg/day to 0.5mg/kg/day. An 89% reduction in total lesions was observed at the 1.0mg/kg/day dose. Although the drug is effective for severe acne, reported side effects may be severe, including inflammation of the lips, which is dose related.

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